

BIBL FILE COPY

Best Available Copy

②

AD-A207 708

AIR FORCE HEALTH STUDY
(PROJECT RANCH HAND II)

**AN EPIDEMIOLOGIC INVESTIGATION
OF HEALTH EFFECTS
IN AIR FORCE PERSONNEL
FOLLOWING EXPOSURE
TO HERBICIDES**

SUMMARY
MORTALITY UPDATE - 1939
17 APRIL 1989

WILLIAM H. WOLFE, COLONEL, USAF, MC
JOEL E. MICHALEK, Ph.D.
JUDSON C. MINER, COLONEL, USAF, BSC

Prepared for:
THE SURGEON GENERAL
UNITED STATES AIR FORCE
BOLLING AFB, D.C. 20332-6188

DTIC
ELECTE
MAY 12 1989

EPIDEMIOLOGY DIVISION
USAF SCHOOL OF AEROSPACE MEDICINE
HUMAN SYSTEMS DIVISION (AFSC)
BROOKS AIR FORCE BASE, TEXAS 78235

20030131095

This document has been approved
for public release and sale in
distribution to customers

SAM/EKS-AY 890227

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE

ADA 207708

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED			1b. RESTRICTIVE MARKINGS		
2a. SECURITY CLASSIFICATION AUTHORITY			3. DISTRIBUTION/AVAILABILITY OF REPORT Approved for public release; distribution is unlimited		
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE			5. MONITORING ORGANIZATION REPORT NUMBER(S)		
4. PERFORMING ORGANIZATION REPORT NUMBER(S) USAFSAM - TR - 89 - 9			7a. NAME OF MONITORING ORGANIZATION The Surgeon General		
5a. NAME OF PERFORMING ORGANIZATION USAF School of Aerospace Medicine		6a. OFFICE SYMBOL (If applicable) USAFSAM/EK		7b. ADDRESS (City, State, and ZIP Code) United States Air Force Bolling Air Force Base, D.C. 20332-6188	
5c. ADDRESS (City, State, and ZIP Code) Human Systems Division (AFSC) Brooks Air Force Base, Texas 78235-5301		8a. NAME OF FUNDING/SPONSORING ORGANIZATION USAF School of Aerospace Medicine		8b. OFFICE SYMBOL (If applicable) USAFSAM/EK	
5c. ADDRESS (City, State, and ZIP Code) Human Systems Division (AFSC) Brooks Air Force Base, Texas 78235-5301		9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER			
5c. ADDRESS (City, State, and ZIP Code) Human Systems Division (AFSC) Brooks Air Force Base, Texas 78235-5301		10. SOURCE OF FUNDING NUMBERS			
		PROGRAM ELEMENT NO. 65306F	PROJECT NO. 2767	TASK NO. 00	WORK UNIT ACCESSION NO. 01
11. TITLE (Include Security Classification) An Epidemiologic Investigation of Health Effects in Air Force Personnel Following Exposure to Herbicides - Mortality Update - Summary 1989					
12. PERSONAL AUTHOR(S) Wolfe, William H., Michalek, Joel E., Miner, Judson C.					
13a. TYPE OF REPORT Interim		13b. TIME COVERED FROM 1979 TO 1987		14. DATE OF REPORT (Year, Month, Day) 1989 April 17	
15. PAGE COUNT 32					
16. SUPPLEMENTARY NOTATION					
17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)		
FIELD	GROUP	SUB-GROUP	Epidemiologic Investigation; Air Force Health Study; Matched Cohort Design; Nonconcurrent Prospective Design; Mortality Study.		
06	05				
19. ABSTRACT (Continue on reverse if necessary and identify by block number)					
<p>The purpose of the Air Force Health Study is to determine whether those individuals involved in the spraying of herbicides in Vietnam during the Ranch Hand operation have experienced any adverse health effects as a result of their participation in that program. The study is designed to evaluate both the mortality (death) and morbidity (disease) in these individuals over a 20-year period beginning in 1982.</p> <p>The Baseline Mortality Report was released in June 1983, the Baseline Morbidity Report in February 1984. Follow-up mortality reports were released in 1984, 1985, and 1986. This study has not demonstrated health effects which can be conclusively attributed to herbicide or dioxin exposure.</p>					
(Continued)					
20. DISTRIBUTION/AVAILABILITY OF ABSTRACT <input checked="" type="checkbox"/> UNCLASSIFIED/UNLIMITED <input type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS			21. ABSTRACT SECURITY CLASSIFICATION UNCLASSIFIED		
22a. NAME OF RESPONSIBLE INDIVIDUAL WILLIAM H. WOLFE, Col, USAF, MC			22b. TELEPHONE (Include Area Code) (512) 536-2604		22c. OFFICE SYMBOL USAFSAM/EK

(Continuation Block 19.)

This report contains analyses of cumulative deaths occurring up to 31 December 1987. These data show no statistical difference between the cumulative mortality of 1,261 Ranch Hands and that of 6,250 matched Comparisons and the entire population of 19,101 Comparisons. To date, 5.8% of the Ranch Hands, 6.02% of the matched Comparisons and 5.44% of the Comparison population have died.

The overall cumulative mortality of the Ranch Hands remains statistically indistinguishable from that of both their matched Comparisons and the entire Comparison population, although there is a statistically significant increasing trend in post-1983 death rates among Ranch Hand flying officers and a statistically significant increase in Ranch Hand digestive system deaths relative to the Comparison population; these findings are not suggestive of a herbicide effect. Ranch Hands are equivalent to all Comparisons in cumulative accidental, malignant neoplasm and circulatory system mortality.

Keywords: exposure biology; agent orange; Ranch Hand;

(KT) ←

Executive Summary

An evaluation of data through 31 December 1987 (certified as of 15 June 1988) has found no statistical difference between the cumulative mortality of 1,261 Ranch Hands, and that of 6,250 matched Comparisons and the entire population of 19,101 Comparisons. The overall adjusted Ranch Hand mortality rate is 2.81 deaths per 1000 person-years and the corresponding rates for the matched Comparisons and Comparison population are 2.74 and 2.87 deaths per 1000 person-years, respectively. To date, 5.87% of the Ranch Hands, 6.02% of the matched Comparisons and 5.44% of the Comparison population have died. The overall adjusted relative risks assessing Ranch Hand mortality with all Comparisons is estimated as 1.01. This represents an increased risk of death of 1%, a difference that has a 95% probability of occurring by chance alone.

This summary is based on a more extensive mortality report released in April 1989. The additional statistical analyses included in that larger report used data from the original 1:5 matched Comparison group. Additional analytic techniques which treated the Ranch Hands and the Comparisons as samples of larger populations were also used. The results of these additional analyses were the same as the results of the analyses presented in this summary. The use of all of the Comparisons and statistical methods that treated them as a population rather than a sample produced the strongest epidemiologic study. Therefore, only these most important analyses were included in this summary.

This evaluation also differs from previous statistical contrasts of Ranch Hand and Comparison mortality in that the mortality experience of the entire Comparison population has been used as the standard for assessing Ranch Hand mortality.

Adjusted cause-specific analyses reveal group equivalence in accidental, malignant neoplasm and circulatory deaths. Digestive system deaths are statistically significantly more frequent in Ranch Hands (unadjusted SMR=2.7, $P=0.01$) relative to the Comparison population. However, five of the six Ranch Hand digestive system deaths were attributable to alcohol consumption and, therefore, this finding is considered unrelated to herbicide exposure.

Restriction to deaths occurring after 1983, however, shows a statistically significant increasing trend in the standardized mortality ratio (SMR), unadjusted for year of birth, during the years 1983 through 1987 among flying officers. This pattern is due to unusually low Ranch Hand death rates prior to 1986 and increased numbers of Ranch Hand circulatory and malignant neoplasm deaths during 1986 and 1987. However, Ranch Hand malignant neoplasm deaths in the flying officers are not restricted to a particular anatomic site or cancer type as would be expected if Herbicide Orange and its dioxin contaminant were exerting a direct effect on malignant disease. Additionally, current 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) assay results suggest that flying officers were among the least exposed of all Ranch Hand personnel. Although they appear unrelated to herbicide exposure, these results remain unexplained at this time. Continued surveillance is indicated to determine if this trend continues.

In conclusion, the overall cumulative mortality of the Ranch Hands remains statistically indistinguishable from that of both their matched Comparisons and the entire Comparison population, although there is a statistically significant increasing trend in post-1983 death rates among Ranch Hand flying officers and a statistically significant increase in Ranch Hand digestive system deaths relative to the Comparison population; these findings are not suggestive of an herbicide effect. Ranch Hands are equivalent to all Comparisons in cumulative accidental, malignant neoplasm and circulatory system mortality.

TABLE OF CONTENTS

	Page
Executive Summary	i
Table of Contents	iii
1. Introduction	1
2. Ranch Hand Versus Comparison Noncause-Specific Analyses	4
3. Cause-Specific Analyses	13
4. Ranch Hand Exposure Analyses	21
5. Conclusion	22
References	24
Principal Investigators	25
Advisory Committee Members	26

Accession For	
NTIS GRA&I	<input checked="" type="checkbox"/>
DTIC TAB	<input checked="" type="checkbox"/>
Unannounced	<input type="checkbox"/>
Justification	
By _____	
Distribution/	
Availability Codes	
Dist	Avail and/or Special
A-1	



1. INTRODUCTION

This report updates the findings of the Air Force Health Study baseline mortality report [1] released on June 30, 1983. Other updates were released in 1984 [2], 1985 [3] and 1986 [4]. The reader is referred to the baseline report for information regarding the study design, the mortality determination process and previous findings.

This report differs from previous reports in that the entire Comparison population has been incorporated in the mortality determination. This expansion has allowed the application of statistical procedures that accommodate population death rates to compare observed and expected numbers of deaths with adjustment for calendar period as well as age at death, rank and occupation. Additionally, small increases in the number of Ranch Hands have occurred as additional Ranch Hands were recently determined to be eligible for inclusion in the study. As these new Ranch Hands were added to the study, newly matched Comparisons were added to the matched Comparison cohort. Thus, the group sizes in this report differ somewhat from those in previous mortality reports. These analyses also differ from those shown in previous reports because tour dates were determined for all Ranch Hands and their matched Comparisons, allowing the appropriate mortality contrasts referenced from date of tour as well as from date of birth.

This summary is based on a more extensive mortality report released in March 1989 and the reader is referred to that report for more detail. The additional statistical analyses included in that larger report used data from the original 1:5 matched Comparison group. Additional analytic techniques which treated the Ranch Hands and the Comparisons as samples of larger populations were also used. The results of these additional analyses were the same as the results of the analyses presented here. The use of all of the Comparisons and statistical methods that treated them as a population rather than a sample produced the strongest epidemiologic study. Therefore, only these most important analyses are included in this summary.

Tour dates for the unmatched Comparisons were randomly generated to permit analyses and report writing to take place while tour date determination for this expanded group continues. These artificial dates were randomly produced and are uniformly distributed over the range November 1956 to October 1971. This range corresponds to the range of matched Comparison tour dates. The effect of the use of these artificial tour dates for unmatched Comparisons is negligible, as evidenced by the near equivalence of Ranch Hand versus Comparison mortality contrasts both with and without the use of tour date information.

This report, therefore, contrasts the mortality of 1,261 Ranch Hands with that of the entire Comparison population of 19,101 Comparisons who flew or serviced C-130 cargo aircraft in Southeast Asia during the same calendar period that the Ranch Hand unit was active in Vietnam. The number of Ranch Hands has increased slightly above the 1,247 included in the Baseline Mortality report of June 1983 because 14 additional men were discovered to have served with the Ranch Hand organization in Vietnam. Except where necessary to relate to the December 1983 report, length of life is measured from the starting date of the qualifying tour of duty, rather than from the birth date, as in previous reports. These new data have allowed the presentation of death rates per person-year, a new statistic in these mortality updates.

The analyses in this report are based on cumulative mortality as of 31 December 1987 (verified as of 15 June 1988). Table 1 shows summary counts, person-years and death rates in deaths per 1000 person-years by group (Ranch Hand, All Comparisons); Table 2 shows these summary statistics by group, rank and occupation. In Tables 1 and 2, the column headed "Rate (%)" shows percent dead [(number dead/number at risk) times 100], a statistic displayed in previous mortality updates and now supplanted by death rate per 1000 person-years. Throughout this report person-years are measured from tour start date. In some tables, columns of death rates per 1000 person-years are simply headed by the word "Rate" (without the % symbol).

A person-year is the length of time lived by one person in one year. The total number of person-years for a cohort is the total length of life lived by the cohort. Persons surviving to the time of data analysis contribute the time in years between the dates of entry into follow-up and data analysis. Persons known to have died before the date of data analysis contribute the time in years between the dates of entry into follow-up and death. In this study, the date of entry into follow-up is the date of the start of the first qualifying tour of duty. The date of data analysis is, effectively, 31 December 1987, the end of the 1987 calendar year. Throughout this report, person-years are rounded to the nearest year.

TABLE 1

Summary Counts by Group, All Personnel

Group	Number at Risk	Number Dead	Rate (%)	Person- years	Rate Per 1000 Person-years
Ranch Hand	1261	74	5.87	24964	2.96
All Comp	19101	1039	5.44	413726	2.51

TABLE 2

Summary Counts by Group, Rank and Occupation

Flying Officers

Group	Number at Risk	Number Dead	Rate (%)	Person- years	Rate Per 1000 Person-years
Ranch Hand	441	25	5.67	8736	2.86
All Comp	5245	319	6.08	110304	2.89

TABLE 2 (Cont'd)

Summary Counts by Group, Rank and Occupation

Enlisted Flyers

Group	Number at Risk	Number Dead	Rate (%)	Person- years	Rate Per 1000 Person-years
Ranch Hand	207	12	5.80	4112	2.92
All Comp	2833	202	7.13	60292	3.35

All Flyers

Group	Number at Risk	Number Dead	Rate (%)	Person- years	Rate Per 1000 Person-years
Ranch Hand	648	37	5.71	12848	2.88
All Comp	8078	521	6.45	170596	3.05

Nonflying Officers

Group	Number at Risk	Number Dead	Rate (%)	Person- years	Rate Per 1000 Person-years
Ranch Hand	26	1	3.85	512	1.95
All Comp	286	15	5.24	6185	2.42

Nonflying Enlisted Personnel

Group	Number at Risk	Number Dead	Rate (%)	Person- years	Rate Per 1000 Person-years
Ranch Hand	587	36	6.13	11604	3.10
All Comp	10737	503	4.68	236945	2.12

All Nonflyers

Group	Number at Risk	Number Dead	Rate (%)	Person- years	Rate Per 1000 Person-years
Ranch Hand	613	37	6.04	12116	3.05
All Comp	11023	518	4.70	243130	2.13

TABLE 2 (Cont'd)

Summary Counts by Group, Rank and Occupation

All Enlisted Personnel

Group	Number at Risk	Number Dead	Rate (%)	Person- years	Rate Per 1000 Person-years
Ranch Hand	794	48	6.05	15716	3.05
All Comp	13570	705	5.19	297237	2.37

All Officers

Group	Number at Risk	Number Dead	Rate (%)	Person- years	Rate Per 1000 Person-years
Ranch Hand	467	26	5.57	9248	2.81
All Comp	5531	334	6.04	116489	2.87

2. RANCH HAND VERSUS COMPARISON NONCAUSE-SPECIFIC ANALYSES

Survival contrasts were carried out between Ranch Hands and the entire population of Comparisons. Each analysis is presented with and without adjustment for the covariates of rank (officer, enlisted), occupation (flying, nonflying) and date of birth. All analyses are unadjusted for race due to the small proportion of blacks.

Figures 1 through 5 show Ranch Hand and Comparison survival curves of the total cohort and in each of the four occupational strata: officers, enlisted, flying personnel and nonflying personnel. In every plot, survival is measured from the start of the qualifying tour. Each curve represents the proportion surviving since the start of the Southeast Asia tour.

Figure 1

Survival Curve Estimates
All Ranch Hands and All Comparisons
Survival from Start of Tour

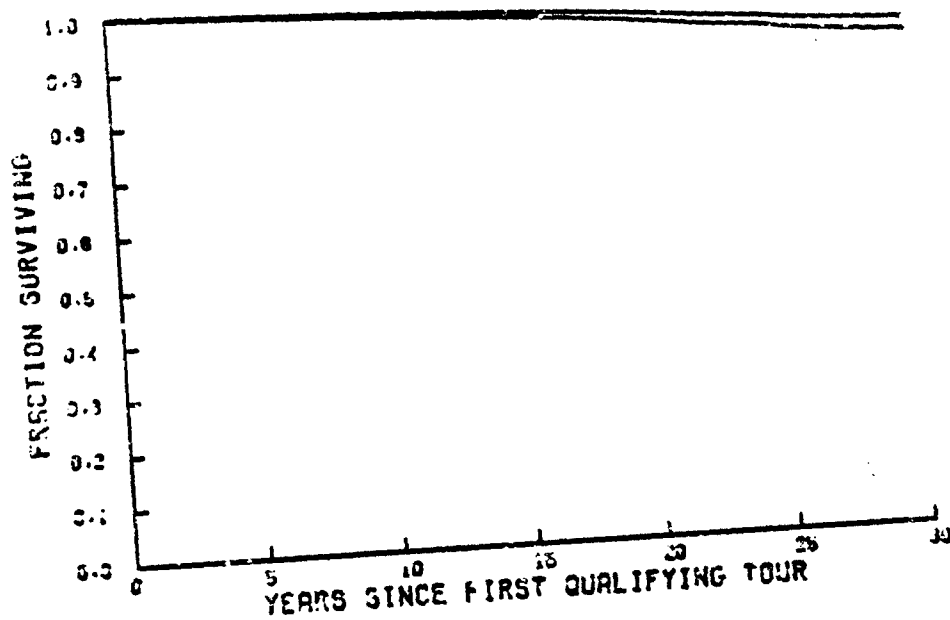


Figure 2

Survival Curve Estimates
Ranch Hand and All Comparison Officers
Survival from Start of Tour

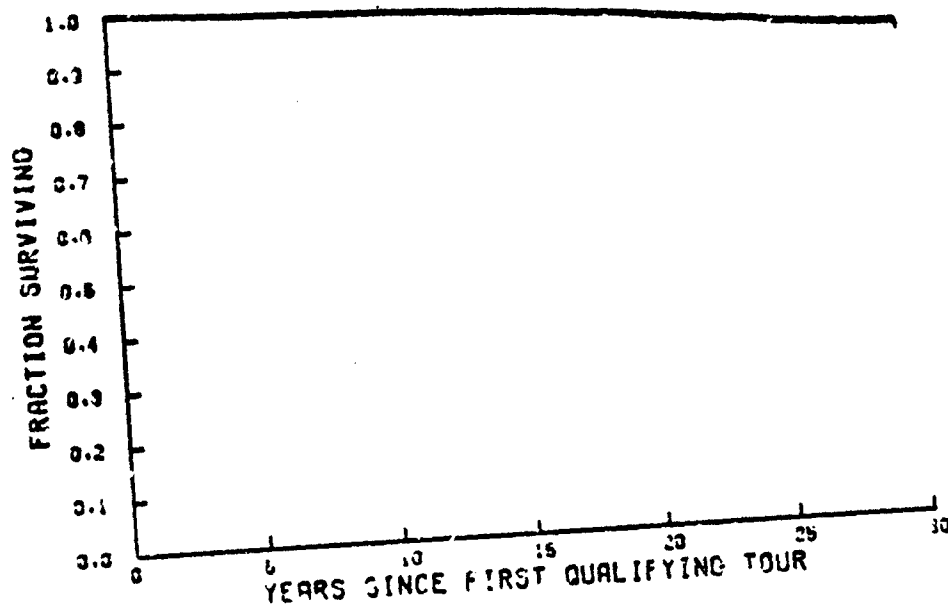


Figure 3

Survival Curve Estimates
Ranch Hand and All Comparison Enlisted Personnel
Survival from Start of Tour

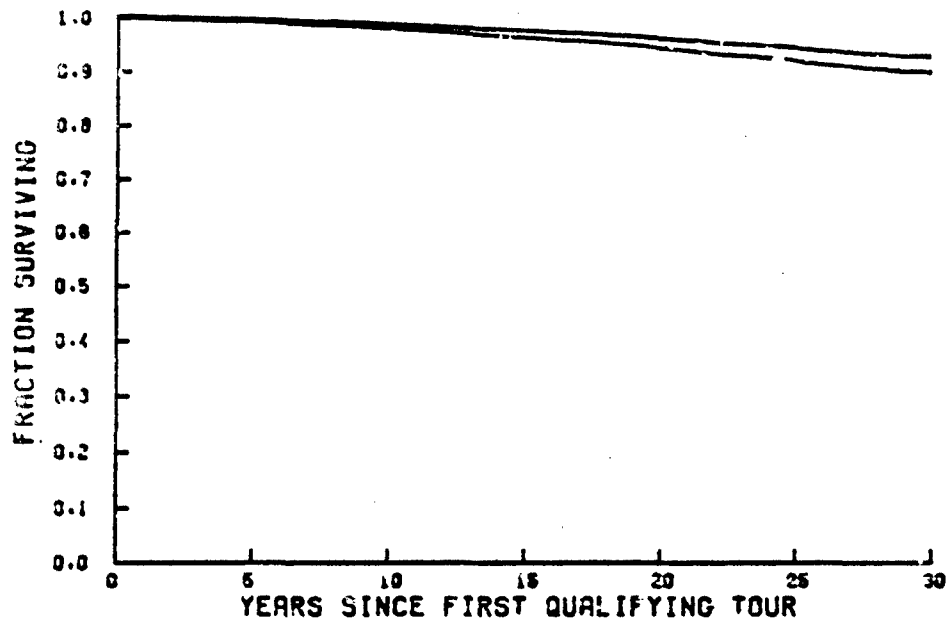


Figure 4

Survival Curve Estimates
Ranch Hand and All Comparison Flyers
Survival from Start of Tour

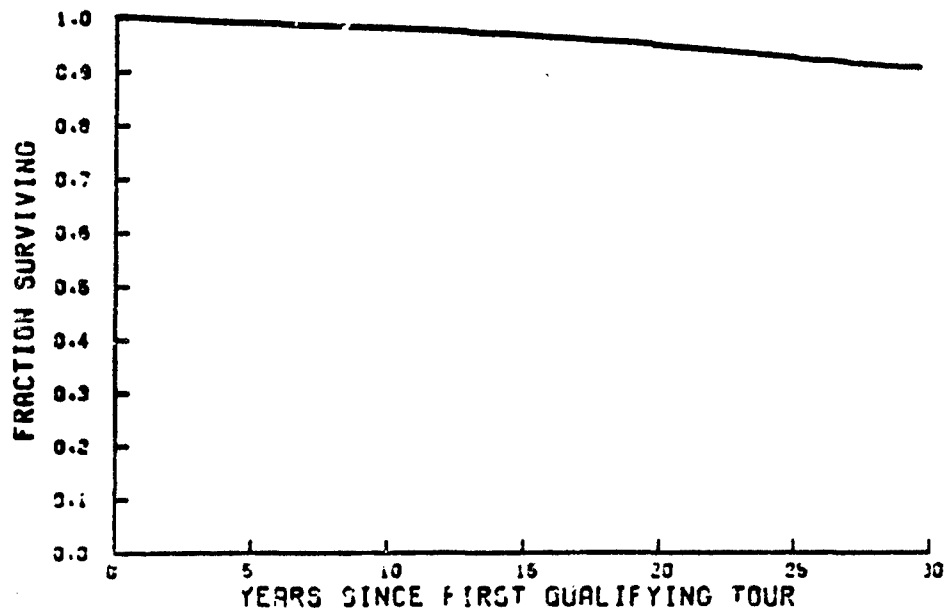
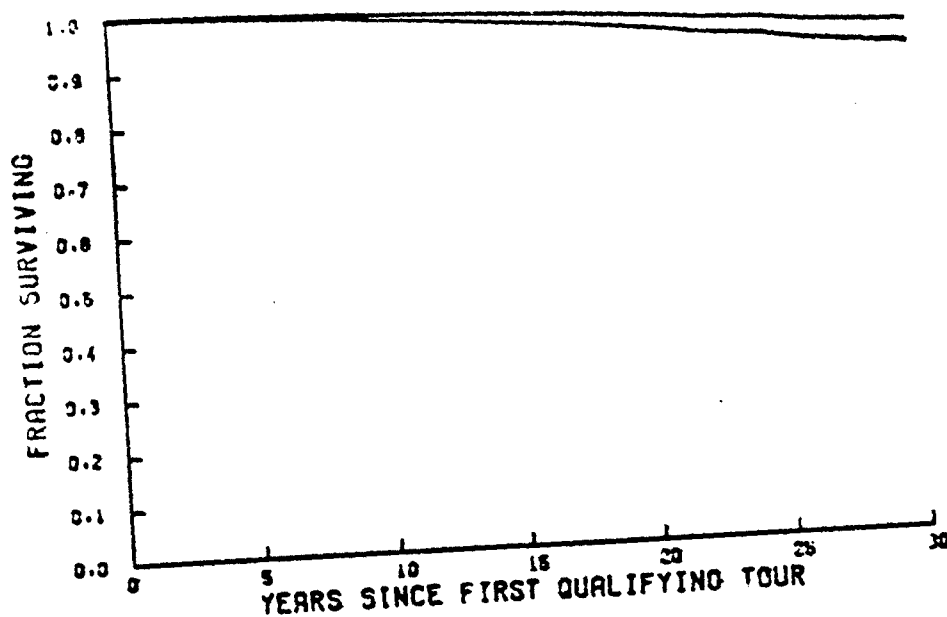


Figure 5

Survival Curve Estimates
Ranch Hand and All Comparison Nonflyers
Survival from Start of Tour



The survival curves are so close together in Figures 2 and 4 that there appears to be only a single curve in each of these figures. This occurred because the relative risks are nearly equal to one.

Unadjusted standardized mortality ratios (SMR), confidence intervals and P-values, contrasting Ranch Hand and Comparison mortality overall and within each of the four occupational groups, are shown in Table 3. The SMR is an estimate of the ratio of the Ranch Hand death rate to the Comparison death rate.

TABLE 3

Unadjusted Odds Ratio Estimates Contrasting
Ranch Hand and All Comparison Mortality,
with Person-years Computed from Tour Start Date

Stratum	Obs	Exp	SMR	P-value
Officer	26	26.5	0.98	0.92
Enlisted	48	38.4	1.24	0.12
Flying	37	39.2	0.94	0.72
Nonflying	37	25.8	1.43	0.03
All Personnel	74	62.7	1.18	0.15

Table 3 demonstrates a near equivalence of Ranch Hand and Comparison mortality without adjustment for covariates, with the exception that the Ranch Hand nonflying personnel are experiencing significantly more deaths than non-flying personnel in the Comparison population (SMR=1.43, P=0.03) in the unadjusted analysis.

Analyses adjusted for the influence of rank, date of birth and occupation, summarized in Table 4, assess Ranch Hand mortality relative to all Comparison death rates in 5-year age and calendar time strata within each of the four rank and occupational strata (officer, enlisted, flying, nonflying) and over the entire Ranch Hand cohort.

TABLE 4

Adjusted Contrasts
Ranch Hands versus All Comparisons

Stratum	Number Dead	Expected Deaths	SMR	95% Confidence Interval	P-value
Officers	26	27.37	0.95	(0.59,1.32)	0.79
Enlisted	48	45.63	1.05	(0.75,1.35)	0.73
Flyers	37	43.19	0.86	(0.58,1.13)	0.35
Nonflyers	37	30.11	1.23	(0.83,1.63)	0.21
All Personnel	74	73.57	1.01	(0.80,1.26)	0.95

After adjustment for rank, date of birth and occupation, Ranch Hand mortality was found to be not significantly different from that expected relative to the Comparison population (Table 4). The number of Ranch Hand deaths was approximately equal to the expected number of deaths among officers and enlisted

personnel. Ranch Hand flyers are experiencing fewer than the expected number of deaths (37 deaths versus 43.19 expected deaths). Ranch Hand nonflyers are experiencing more than the expected number of deaths (37 versus 30.11). The overall cumulative Ranch Hand mortality (74 deaths) is approximated by the expected number (73.57) of deaths.

The previous adjusted contrasts (Table 4), although fully accounting for the effects of rank, occupation and the year of birth, may not detect very recent trends. Therefore, chi-square tests for trend were applied to assess the presence of post-1983 trends in the SMR. These analyses were carried out twice, first with each of the years 1983 through 1987 considered separately and again with 1983 through 1985 collapsed to a single stratum and 1986 and 1987 collapsed to a second single stratum. The results are shown in Table 5. All analyses are conditioned on survival to 1983 and, due to data sparseness, are not adjusted for date of birth. The tests will detect both upward or downward trends in the SMR. To detect upward trends, divide the P-value by 2 when an increasing trend is apparent and replace the P-value by 1.00 when a decreasing trend is apparent. These data were not assessed relative to the Air Force exposure index due to sparseness.

TABLE 5
Ranch Hand Mortality
Five-Year Trend Analysis versus All Comparison

Flying Officers

Chi-square (single year)=4.89 P=0.03
Chi-square (83-85,86-87)=6.10 P=0.01

Year	Number Dead	Rate Per 1000 Person-Years	Expected Deaths	SMR
1983	0	0.00	1.87	0.00
1984	1	2.35	1.70	0.59
1985	1	2.35	1.45	0.69
1986	5	11.84	1.79	2.30
1987	4	9.54	2.29	1.75

Enlisted Flyers

Chi-square (single year)=0.16 P=0.69
Chi-square (83-85,86-87)=0.09 P=0.76

Year	Number Dead	Rate Per 1000 Person-Years	Expected Deaths	SMR
1983	1	5.03	1.03	0.97
1984	0	0.00	0.89	0.00
1985	1	5.07	0.89	1.13
1986	1	5.08	1.34	0.75
1987	1	5.11	0.74	1.35

TABLE 5 (Cont'd)

Ranch Hand Mortality
Five-Year Trend Analysis versus All Comparison

All Flyers

Chi-square (single year)=4.75 P=0.03
Chi-square (83-85,86-87)=5.27 P=0.02

Year	Number Dead	Rate Per 1000 Person-Years	Expected Deaths	SMR
1983	1	1.60	2.92	0.34
1984	1	1.60	2.60	0.38
1985	2	3.21	2.36	0.85
1986	6	9.70	3.17	1.89
1987	5	8.13	3.00	1.67

Nonflying Officers

Year	Number Dead	Rate Per 1000 Person-Years	Expected Deaths	SMR
1983	0	0.00	0.00	0.00
1984	0	0.00	0.09	0.00
1985	0	0.00	0.09	0.00
1986	0	0.00	0.18	0.00
1987	0	0.00	0.37	0.00

Nonflying Enlisted Personnel

Chi-square (single year)=0.01 P=0.93
Chi-square (83-85,86-87)=0.21 P=0.65

Year	Number Dead	Rate Per 1000 Person-Years	Expected Deaths	SMR
1983	2	3.58	1.24	1.62
1984	0	0.00	1.88	0.00
1985	2	3.59	2.21	0.90
1986	3	5.42	1.88	1.59
1987	1	1.81	1.99	0.50

TABLE 5 (Cont'd)

Ranch Hand Mortality
Five-Year Trend Analysis versus All Comparison

All Nonflyers

Chi-square (single year)=0.03 P=0.86
Chi-square (83-85,86-87)=0.13 P=0.71

Year	Number Dead	Rate Per 1000 Person-Years	Expected Deaths	SMR
1983	2	3.43	1.26	1.59
1984	0	0.00	1.97	0.00
1985	2	3.44	2.30	0.87
1986	3	5.19	2.03	1.48
1987	1	1.74	2.24	0.45

All Officers

Chi-square (single year)=4.22 P=0.04
Chi-square (83-85,86-87)=5.38 P=0.02

Year	Number Dead	Rate Per 1000 Person-Years	Expected Deaths	SMR
1983	0	0.00	1.88	0.00
1984	1	2.22	1.79	0.56
1985	1	2.22	1.54	0.65
1986	5	11.18	1.96	2.55
1987	4	9.01	2.64	1.51

All Enlisted Personnel

Chi-square (single year)=0.02 P=0.89
Chi-square (83-85,86-87)=0.30 P=0.58

Year	Number Dead	Rate Per 1000 Person-Years	Expected Deaths	SMR
1983	3	3.96	2.14	1.40
1984	0	0.00	2.72	0.00
1985	3	3.98	3.08	0.97
1986	4	5.33	3.07	1.30
1987	2	2.68	2.72	0.73

TABLE 5 (Cont'd)

Ranch Hand Mortality
Five-Year Trend Analysis versus All Comparison

All Personnel

Chi-square (single year)=2.70 P=0.10
Chi-square (83-85,86-87)=4.31 P=0.04

Year	Number Dead	Rate Per 1000 Person-Years	Expected Deaths	SMR
1983	3	2.48	3.88	0.77
1984	1	0.83	4.48	0.22
1985	4	3.32	4.68	0.85
1986	9	7.52	5.01	1.80
1987	6	5.04	5.13	1.17

The increased risks specific to the calendar years 1986 and 1987 for flyers shown in Table 5 are seen to produce an increasing trend from 1983 through 1987, with the respective SMR's being 0.34, 0.38, 0.85, 1.89, and 1.67. This trend is statistically significant. The trend within the flyers is due to an increasing trend in the SMR within the flying officer stratum, with no trend apparent within the enlisted flyer stratum. No trends are apparent or are detected in the nonflying or enlisted strata.

The trend is caused as much by the increased deaths in 1986 and 1987 as by the decreased deaths in the flying officers prior to 1986. Of the 5 flying officer Ranch Hand deaths during 1986, 3 were due to malignant neoplasm (SMR=3.92), 1 was a circulatory system death (SMR=1.68) and 1 was due to unknown causes (SMR not defined). Of the 4 deaths within the Ranch Hand flying officers occurring during 1987, 1 was accidental (SMR=6.00), 1 was due to a malignant neoplasm (SMR=0.98) and 2 were due to diseases of the circulatory system (SMR=2.62). The single Ranch Hand flying officer death during 1984 was due to circulatory system disease (SMR=2.35) and the single death occurring during 1985 was due to a malignant neoplasm (SMR=2.35). The observed Ranch Hand malignant neoplasm deaths during 1983 through 1987 among flyers or flying officers were not restricted to a particular anatomic site or morphological type.

The observed statistically significant increasing trend in the SMR among flying officers is of concern and emphasizes the importance of continued mortality surveillance. However, it appears due to recent elevations in Ranch Hand circulatory and malignant neoplasm death rates with no apparent pattern by anatomic site or morphology among those deaths due to malignant neoplasm. If herbicide exposure were having a direct effect on malignant disease, one would anticipate a clustering by site or type of cancer. The implication of these observations is as yet unclear. Further, the trend is not expected in

relation to known TCDD body burdens among living Ranch Hands currently being assayed. Those assays suggest that flying officers were among the least exposed Ranch Hands; the heaviest exposure occurred in nonflying enlisted personnel. Although it appears unrelated to herbicide exposure, the finding currently remains unexplained. The analyses shown in Table 5 will be repeated in the next mortality report.

Graphical techniques to identify clustering of deaths by age or in time were carried out and revealed no evidence of clustering.

3. CAUSE-SPECIFIC ANALYSES

Table 6 shows death counts and death rates (deaths per 1000 person-years) referenced to the start of the qualifying tour by cause and subgroup. The death rate units are deaths per 1000 person-years.

TABLE 6
Deaths and Death Rates by Cause and Group
Flying Officers

	Ranch Hand		All Comparison	
	No.	Rate	No.	Rate
Accidental	9	1.03	93	0.84
Suicide	0	0.00	15	0.14
Homicide	0	0.00	3	0.03
Infections, Parasitic	0	0.00	2	0.02
Neoplasm, Malignant	5	0.57	79	0.72
Neoplasms, Uncertain	0	0.00	2	0.02
Endocrine	0	0.00	1	0.01
Blood, Blood Forming	0	0.00	1	0.01
Mental Disorders	0	0.00	2	0.02
Nervous System	0	0.00	4	0.04
Circulatory System	8	0.92	97	0.88
Respiratory System	0	0.00	5	0.05
Digestive	2	0.23	11	0.10
Genitourinary System	0	0.00	1	0.01
Congenital Anomalies	0	0.00	1	0.01
Ill-Defined	0	0.00	2	0.02
Unknown	1	0.11	0	0.00
Total	25		319	

TABLE 6 (Cont'd)

Deaths and Death Rates by Cause and Group

Enlisted Flyers

	Ranch Hand		All Comparison	
	No.	Rate	No.	Rate
Accidental	4	0.97	67	1.11
Suicide	1	0.24	17	0.28
Homicide	0	0.00	3	0.05
Infections, Parasitic	0	0.00	1	0.02
Neoplasm, Malignant	1	0.24	39	0.65
Endocrine	0	0.00	1	0.02
Nervous System	0	0.00	1	0.02
Circulatory System	2	0.49	54	0.90
Respiratory System	0	0.00	3	0.05
Digestive	2	0.49	11	0.18
Congenital Anomalies	0	0.00	1	0.02
Ill-Defined	2	0.49	3	0.05
Unknown	0	0.00	1	0.02
Total	12		202	

All Flyers

	Ranch Hand		All Comparison	
	No.	Rate	No.	Rate
Accidental	13	1.01	160	0.94
Suicide	1	0.08	32	0.19
Homicide	0	0.00	6	0.04
Infections, Parasitic	0	0.00	3	0.02
Neoplasm, Malignant	6	0.47	118	0.69
Neoplasms, Uncertain	0	0.00	2	0.01
Endocrine	0	0.00	2	0.01
Blood, Blood Forming	0	0.00	1	0.01
Mental Disorders	0	0.00	2	0.01
Nervous System	0	0.00	5	0.03
Circulatory System	10	0.78	151	0.89
Respiratory System	0	0.00	8	0.05
Digestive	4	0.31	22	0.13
Genitourinary System	0	0.00	1	0.01
Congenital Anomalies	0	0.00	2	0.01
Ill-Defined	2	0.16	5	0.03
Unknown	1	0.08	1	0.01
Total	37		521	

TABLE 6 (Cont'd)

Deaths and Death Rates by Cause and Group

Nonflying Officers

	Ranch Hand		All Comparison	
	No.	Rate	No.	Rate
Accidental	0	0.00	1	0.16
Suicide	1	1.95	1	0.16
Neoplasm, Malignant	0	0.00	5	0.81
Circulatory System	0	0.00	7	1.13
Digestive	0	0.00	1	0.16
Total	1		15	

Nonflying Enlisted

	Ranch Hand		All Comparison	
	No.	Rate	No.	Rate
Accidental	9	0.78	129	0.54
Suicide	1	0.09	41	0.17
Homicide	2	0.17	14	0.06
Infections, Parasitic	0	0.00	6	0.03
Neoplasm, Malignant	6	0.52	103	0.43
Neoplasms, Uncertain	0	0.00	1	0.00
Endocrine	1	0.09	1	0.00
Blood, Blood Forming	0	0.00	1	0.00
Mental Disorders	0	0.00	7	0.03
Nervous System	0	0.00	7	0.03
Circulatory System	15	1.29	151	0.64
Respiratory System	0	0.00	14	0.06
Digestive	2	0.17	14	0.06
Genitourinary System	0	0.00	8	0.03
Ill-Defined	0	0.00	5	0.02
Unknown	0	0.00	1	0.00
Total	36		563	

TABLE 6 (Cont'd)

Deaths and Death Rates by Cause and Group

All Nonflying

	Ranch Hand		All Comparison	
	No.	Rate	No.	Rate
Accidental	9	0.74	130	0.53
Suicide	2	0.17	42	0.17
Homicide	2	0.17	14	0.06
Infections, Parasitic	0	0.00	6	0.02
Neoplasia, Malignant	6	0.50	108	0.44
Neoplasms, Uncertain	0	0.00	1	0.00
Endocrine	1	0.08	1	0.00
Blood, Blood Forming	0	0.00	1	0.01
Mental Disorders	0	0.00	7	0.03
Nervous System	0	0.00	7	0.03
Circulatory System	15	1.24	158	0.65
Respiratory System	0	0.00	14	0.06
Digestive	2	0.17	15	0.06
Genitourinary System	0	0.00	8	0.03
Ill-Defined	0	0.00	5	0.02
Unknown	0	0.00	1	0.00
Total	37		518	

All Personnel

	Ranch Hand		All Comparison	
	No.	Rate	No.	Rate
Accidental	22	0.88	290	0.70
Suicide	3	0.12	74	0.18
Homicide	2	0.08	20	0.05
Infections, Parasitic	0	0.00	9	0.02
Neoplasm, Malignant	12	0.48	226	0.55
Neoplasms, Uncertain	0	0.00	3	0.01
Endocrine	1	0.04	3	0.01
Blood, Blood Forming	0	0.00	2	0.00
Mental Disorders	0	0.00	9	0.02
Nervous System	0	0.00	12	0.03
Circulatory System	25	1.00	309	0.75
Respiratory System	0	0.00	22	0.05
Digestive	6	0.24	37	0.09
Genitourinary System	0	0.00	9	0.02
Congenital Anomalies	0	0.00	2	0.00
Ill-Defined	2	0.08	10	0.02
Unknown	1	0.04	2	0.00
Total	74		1039	

Unadjusted group contrasts are shown in Table 7.

TABLE 7
Unadjusted Group Contrasts by Cause of Death
Ranch Hands versus All Comparisons

	Dead	Expected	SMR	95% Conf. Interval	P-value
Accidental	22	17.50	1.26	(0.73, 1.78)	0.28
Suicide	3				
Homicide	2				
Infections, Parasitic	0				
Neoplasm, Malignant	12	13.64	0.88	(0.38, 1.38)	0.66
Neoplasms, Uncertain	0				
Endocrine	1				
Blood, Blood Forming	0				
Mental Disorders	0				
Nervous System	0				
Circulatory System	25	18.64	1.34	(0.82, 1.87)	0.14
Respiratory System	0				
Digestive	6	2.23	2.69	(1.00, 5.85)	0.01
Genitourinary System	0				
Congenital Anomalies	0				
Ill-Defined	2				
Unknown	1				

The unadjusted analysis of deaths by cause indicates a significant elevation (SMR=2.7, P=0.01) of the Ranch Hand SMR for digestive system deaths. However, 5 of the 6 Ranch Hand digestive system deaths were attributable to alcohol consumption and, therefore, this finding is considered unrelated to herbicide exposure. The 6 Ranch Hand digestive system deaths are distributed by rank and occupation as 2 flying officers, 2 flying enlisted and 2 nonflying enlisted. Ranch Hand accidental, malignant neoplasm and circulatory system mortality was found to be not significantly different from that expected relative to the Comparison population.

Adjusted analyses contrasting Ranch Hands with all Comparisons on accidental, malignant neoplasm and circulatory deaths were carried out with person-years computed from tour start date. Similar analyses of digestive system deaths could not be carried out since the number of Ranch Hand digestive system deaths (6) were too few for meaningful adjustment. These analyses are adjusted for date of birth, survival time, calendar time, rank and occupation. The results are summarized in Tables 8, 9 and 10.

TABLE 8

Adjusted Contrasts of Ranch Hands and
All Comparisons on Accidental Deaths

Stratum	Number Dead	Expected Deaths	SMR	95% Confidence Interval	P-value
Officers	9	7.35	1.23	(0.43,2.03)	0.54
Enlisted	13	10.99	1.18	(0.54,1.83)	0.54
Flyers	13	11.89	1.09	(0.50,1.69)	0.75
Nonflyers	9	6.98	1.29	(0.45,2.13)	0.44
All Personnel	22	18.02	1.16	(0.64,2.36)	0.54

In the adjusted analysis of accidental deaths summarized in Table 8, the SMR did not change significantly with rank and/or occupation. No significant group differences were detected.

TABLE 9

Adjusted Contrasts of Ranch Hands and
All Comparisons On Malignant Neoplasm Deaths

Stratum	Number Dead	Expected Deaths	SMR	95% Confidence Interval	P-value
Officers	5	6.99	0.71	(0.09,1.34)	0.45
Enlisted	7	9.88	0.71	(0.18,1.23)	0.36
Flyers	6	10.45	0.57	(0.12,1.03)	0.17
Nonflyers	6	6.44	0.93	(0.19,1.68)	0.86
All Personnel	12	16.95	0.70	(0.40,1.24)	0.23

In the adjusted analysis of malignant neoplasm deaths summarized in Table 9, the SMR did not change significantly with rank and/or occupation. No significant group differences were detected.

TABLE 10

Adjusted Contrasts of Ranch Hands and
All Comparisons on Circulatory Deaths

Stratum	Number Dead	Expected Deaths	SMR	95% Confidence Interval	P-value
Officers	8	8.58	0.93	(0.29,1.58)	0.84
Enlisted	17	14.61	1.17	(0.62,1.73)	0.51
Flyers	10	13.17	0.76	(0.29,1.23)	0.39
Nonflyers	15	9.83	1.53	(0.75,2.30)	0.10
All Personnel	25	23.68	1.09	(0.73,1.61)	0.67

In the adjusted analysis of Ranch Hand circulatory deaths summarized in Table 10, the SMR did not change significantly with rank and/or occupation. No significant group differences were detected.

Cumulative digestive system mortality is shown in Table 11.

TABLE 11

Group Cumulative Site-specific Digestive System Mortality

Category	Number of Deaths	
	Ranch Hand	All Comp
Alcoholic Liver Disease	5	23
Nonalcoholic Liver Disease	0	5
Other Liver Disease	1	1
Esophagus, Stomach and Duodenum	0	4
Other Intestinal Disease	0	4
Totals	6	37

Five (83%) of the six digestive system deaths in the Ranch hand group were liver-related; all five (100%) of these were attributable to alcohol consumption. Twenty-nine of the 37 Comparison digestive system deaths (79%) were liver related; 23 of the 29 liver-related deaths (79%) were attributable to alcohol consumption. Ranch Hand digestive system mortality during 1986 and 1987, as well as during 1983, 1984 and 1985, is unremarkable since the last Ranch Hand digestive system death occurred in 1985. Digestive system deaths did not, therefore, contribute to the already noted (Table 5) increased Ranch Hand mortality during 1986 and 1987.

Table 12 shows cumulative site-specific malignant neoplasm mortality by group.

TABLE 12

Group Cumulative Site-specific Neoplasm Mortality

Category	Number of Deaths	
	Ranch Hand	All Comp
Lip, Oral Cavity and Pharynx	0	11
Digestive Organs and Peritoneum Including Cancers of the Stomach, Pancreas and Colon	3	50
Respiratory and Intrathoracic Organs Including Lung	5	85
Bone, Connective Tissue, Skin and Breast	1	12
Genitourinary Organs Including Cancers of the Kidneys, Bladder, Testicles and Prostate Gland	1	8
Other and Unspecified Sites	2	38
Lymphatic and Hematopoietic Tissue Including Hodgkin's Disease, Leukemia and Lymphoma	0	22
Benign Neoplasms	0	1
Neoplasms of Unspecified Nature	0	2
Total	12	229

Table 12 shows that the malignant neoplasm deaths appear to be widely distributed by site with approximately one third (33%) occurring in the lung in both groups. Within-year patterns were also similarly distributed.

With regard to cell type, the 12 Ranch Hand malignant neoplasm deaths appear widely distributed in a pattern similar to that of the Comparisons, both cumulatively and within calendar year.

In summary, an elaboration of Ranch Hand and Comparison digestive deaths by site and malignant neoplasm deaths by site and morphology revealed no unusual pattern of Ranch Hand deaths relative to the mortality experience of all Comparisons.

4. RANCH HAND EXPOSURE ANALYSES

Analyses were carried out within each level of rank (officer, enlisted) to assess whether the Ranch Hand versus Comparison mortality contrast changed with level of exposure to dioxin (TCDD). Person-years were computed from tour start date. The results are summarized in Table 13.

TABLE 13

Ranch Hand Exposure within Officers and within Enlisted Person-years Assessment Relative to All Comparisons

Officers

Exposure	Number of Deaths	Adjusted Expected Deaths	Adjusted SMR
Low	7	7.52	0.93
Medium	10	10.16	0.98
High	9	9.69	0.93

Contrast	Relative Risk	P-value
Medium versus Low and High	1.06	0.91
High versus Low and Medium	1.00	1.00

Enlisted Personnel

Exposure	Number of Deaths	Adjusted Expected Deaths	Adjusted SMR
Low	17	14.70	1.16
Medium	13	13.78	0.94
High	18	17.56	1.03

Contrast	Relative Risk	P-value
Medium versus Low and High	0.82	0.58
High versus Low and Medium	0.89	0.72

Both analyses failed to reveal any relationship between mortality and the exposure index.

Unpublished dioxin assay results suggest that the Air Force exposure index is not a valid measure of exposure to TCDD. The relationship between this index and dioxin body burden in living Ranch Hands will be described in a forthcoming report.

5. CONCLUSION

An evaluation of cumulative and noncause-specific mortality revealed no statistically significant differences between Ranch Hands and all Comparisons, after adjustment for rank, occupation, date of birth, and calendar time in 5 year intervals.

The adjusted cause-specific analyses are summarized in Table 14. Only accidental, malignant neoplasm and circulatory deaths were numerous enough to permit adjusted analyses. None of the adjusted odds ratios shown in Table 14 are statistically different from one.

TABLE 14

Adjusted Cause-specific Summary
Ranch Hand versus All Comparison

Accidental, Malignant Neoplasm and Circulatory Deaths

Cause	SMR
Accidental	1.16
Malignant neoplasms	0.70
Circulatory system	1.09

In an unadjusted analysis, Ranch Hands were found to have experienced significantly more digestive system deaths than the Comparisons ($SMR=2.7, P=0.01$). However, five of the six Ranch Hand digestive system deaths were attributable to alcohol consumption and, therefore, this finding is considered unrelated to herbicide exposure.

Restriction to deaths occurring after 1983 shows a statistically significant increasing trend in the SMR, unadjusted for year of birth, during the years 1983 through 1987 among flying officers. This pattern is due to unusually low Ranch Hand death rates prior to 1986 and increased numbers of Ranch Hand circulatory and malignant neoplasm deaths during 1986 and 1987. However, Ranch Hand malignant neoplasm deaths in the flying officers are not restricted to a particular anatomic site or cancer type as would be expected if Herbicide Orange and its dioxin contaminant were exerting a direct effect on malignant disease. Additionally, current TCDD assay results suggest that flying officers were among the least exposed of all Ranch Hand personnel. Although they do not appear related to herbicide exposure, these results remain unexplained at this time. Continued surveillance is indicated to determine whether this trend continues.

An analysis of Ranch Hand mortality versus dioxin exposure, as estimated by the Air Force exposure index, revealed no association between mortality and exposure.

In conclusion, the overall cumulative mortality of the Ranch Hands remains statistically indistinguishable from that of both their matched Comparisons and the entire Comparison population, although there is a statistically significant increasing trend in post-1983 death rates among Ranch Hand flying officers and a statistically significant increase in Ranch Hand digestive system deaths relative to the Comparison population; these findings are not suggestive of a herbicide effect. Ranch Hands are equivalent to all Comparisons in cumulative accidental, malignant neoplasm and circulatory system mortality.

REFERENCES

1. Lathrop, G.D., Moynahan, P.M., Wolfe, W.H., Albanese, R.A. (1983). An epidemicologic investigation of health effects in Air Force personnel following exposure to herbicides: baseline mortality results. USAF School of Aerospace Medicine, Brooks AFB, Texas. 61 pp. Available from NTIS, Springfield, Virginia. (Accession document no. AD A-130-793).
2. Wolfe, W.H., Michalek, J.E., Albanese, R.A., Lathrop, G.D., and Moynahan, P.M. (1984). An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: mortality update-1984. USAF School of Aerospace Medicine, Brooks AFB, Texas. 46 pp. Available from NTIS, Springfield, Virginia. (Accession document no. AD A-162-687).
3. Wolfe, W.H. and Michalek, J.E. (1985). An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: mortality update-1985. USAF School of Aerospace Medicine, Brooks AFB, Texas. 43 pp. Available from NTIS, Springfield, Virginia. (Accession document no. AD A-163-237).
4. Wolfe, W.H., Michalek, J.E., Miner, J.C. and Peterson, M.R. (1986). An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: mortality update-1986. USAF School of Aerospace Medicine, Brooks AFB, Texas. 7 pp. Available from NTIS, Springfield, Virginia. (Accession document no. AD A-175-453).

Principal Investigators

William H. Wolfe, MD, MPH, FACPM
Colonel, USAF, MC
Chief, Epidemiology Division

Joel E. Michalek, PhD, GM-14
Chief, Biometrics Branch
Epidemiology Division

Judson C. Miner, DVM, MPH, ACVPM
Colonel, USAF, BSC
Chief, Special Projects Branch
Epidemiology Division

Coinvestigator

Mr Vincent Elequin
Medical Records Administrator
Special Projects Branch
Epidemiology Division

Contributor

Mr Thomas White
Senior Subject Matter Specialist
Biometrics Branch
Epidemiology Division

Advisory Committee on Special Studies
Relating to the Possible Long-term Health Effects
of Phenoxy Herbicides and Contaminants

Committee Members

Robert W. Miller, M.D., M.P.H., Dr. P.H.
Chairman
Chief, Clinical Epidemiology Branch
Executive Plaza North, Room 400
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20205
Tel: (301) 496-5785

Julianne Byrne, Ph.D.
Clinical Epidemiology Branch
Executive Plaza North, Room 400
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20205
Tel: (301) 496-5785

Kathleen Kreiss, M.D.
Director, Occupational Medicine
Program
National Jewish Center for
Immunology and Respiratory Medicine
3800 E. Colfax Ave
Denver, Colorado 80206
Tel: (303) 398-1525

George W. Comstock, M.D., M.P.H.,
Dr. P.H., F.A.C.E.
Alumni Centennial Professor
of Epidemiology
The Johns Hopkins University
School of Hygiene and Public Health
Training Center for Public Health
Research
Box 2067
Hagerstown, Maryland 21742-2067
Tel: (301) 791-3230

Leonard T. Kurland, M.D., Dr. P.H.
Senior Consultant and Professor
of Epidemiology
Department of Health Sciences
Research
Mayo Clinic
200 First Street, S.W.
Rochester, Minnesota 55905
Tel: (507) 284-5540

Jack Friedman, M.D., Ph.D.
Grace Hospital
4490 Oak Street
Vancouver, British Columbia
V6H-3V5
CANADA
Tel: (604) 228-2749

Richard R. Monson, M.D., Sc.D.
Department of Epidemiology
Harvard School of Public Health
677 Huntington Avenue
Boston, Massachusetts 02115
Tel: (617) 732-1050

Norton Nelson, Ph.D.
Department of Environmental Medicine
New York University School of Medicine
New York, New York 10016
Tel: (914) 351-2566

Craig T. Ramey, Ph.D.
Director of Research
Frank Porter Graham Child
Development Center
University of North Carolina
54 Bypass
Chapel Hill, North Carolina 27514
Tel: (919) 966-4121

Peter O'Brien, Ph.D.
Department of Health Sciences Research
Section of Biostatistics
Mayo Clinic
200 First Street, S.W.
Rochester, Minnesota 55905
Tel: (507) 284-2511